I. Research Involving Human Subjects

A. Introduction

The Advanced Technology Program (ATP) will fund research involving human subjects. Research involving human subjects must comply with all applicable federal statutes, Executive Orders, federal regulations, and policies. Applicable authorities are listed in Appendix 1.

For certain types of research involving human subjects, the National Institute of Standards and Technology (NIST) has procedures that require NIST as an institution to approve documentation in addition to ATP review and approval.

The Federal Policy for the Protection of Human Subjects (the Common Rule), adopted by the Department of Commerce (DOC) at 15 C.F.R. Part 27, sets forth the appropriate policies and procedures for the protection of human subjects in research. The Common Rule is available at http://www.access.gpo.gov/nara/cfr/cfr-table-search.html.[1]

The Common Rule defines *human subject* as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information. The term *research* means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

The Common Rule provides a systematic means, based on established, internationally recognized ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities. An awardee institution bears the responsibility for safeguarding the rights and welfare of human subjects in DOC-supported research.

To help you determine whether your research includes the use of human subjects, you are encouraged to review the Human Subjects Determination Checklist in Appendix 2 before submitting your proposal to ATP.

B. Assurance of Compliance

Applicant organizations proposing to involve human subjects in nonexempt research must have on file a written assurance approved for federalwide use from the Office for Human Research Protections (OHRP) within the Department of Health and Human Services (DHHS).

[1] Websites listed in this publication are accurate as of the publishing date. Check www.atp.nist.gov/atp/helpful.htm for updates to websites.

The Common Rule at section 27.103(a) requires that each institution engaged in federally supported human subject research file an assurance of compliance. An assurance formalizes the institution's commitment to protect human subjects.

Under the Common Rule at section 27.102(f), awardees and their collaborating institutions become engaged in human subject research whenever their employees or agents (1) obtain data through intervention or interaction with living individuals for research purposes or (2) obtain identifiable private information for research purposes.

Awardee institutions are considered to be engaged in human subject research whenever they receive a direct DOC award to support such research, even when all activities involving human subjects are carried out by a joint venture partner, subcontractor, or formal collaborator. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.

Awardees are also responsible for ensuring that each joint venture partner, subcontractor, and formal collaborating institution that is engaged in human subject research hold an assurance approved for federalwide use from OHRP.

ATP will accept either a current Federalwide Assurance (FWA) or a current Multiple Project Assurance (MPA) from OHRP. ATP does not grant or accept a Single Project Assurance (SPA). Information regarding the FWA process can be found at http://ohrp.osophs.dhhs.gov/humansubjects/assurance/fwas.htm.

C. Protected Classes

Research involving pregnant women, human fetuses, neonates, prisoners, or children must comply with 45 C.F.R. Part 46 Subparts B, C, and D, respectively, which describe additional protections required for these human subjects.

NIST considers all custom collection of gestational tissues (e.g., yolk sac) or cells to be covered by subpart B.

The regulations for research involving the protected classes identified in subparts B, C, and D can be found at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm.

The use of cadaveric materials is governed by applicable state and local laws and is not directly regulated by the Common Rule.

D. Clinical Trials

On a case-by-case basis, ATP may support research as part of a Phase I clinical trial. ATP expects requests to support Phase I clinical trials to be rare. If the research proposed includes all or any portion of a Phase I clinical trial, the research must be deemed consistent with all ATP requirements for scientific and technological merit selection criteria. Although the criteria may be met, ATP reserves the right not to fund the Phase I clinical trial, and ATP may ask the proposer to describe the impact on the project if that activity is removed from the project.

Under no circumstances will ATP support research included in a Phase II, Phase III, or Phase IV clinical trial.

E. Human Subjects in Foreign Countries

Generally, ATP does not fund research involving human subjects in foreign countries. ATP will consider, however, the use of tissue, cells, or data from a foreign source on a limited basis if all of the following criteria are satisfied:

1. the scientific source is considered unique,
2. an equivalent source is unavailable within the United States,
3. an alternative approach is not scientifically of equivalent merit, and
4. the specific use qualifies for an exemption from the Common Rule.

F. Transplantation of Fetal Tissue

Research involving the transplantation of human fetal tissue must meet all of the requirements set forth at section 498A(b) and (c) of the Public Health Service Act, 42 U.S.C. §§ 289g(b) and (c), and section 111 of the NIH Revitalization Act of 1993, 42 U.S.C. § 289(g)1. Guidance can be found at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/publiclaw103-43.htm.

G. Research Involving Embryos and Embryonic Stem Cells

ATP adheres to all federal statutes, Executive Orders, federal regulations, and policies regarding the use of human embryos and human embryonic stem cells.

Although other federal agencies may permit the use of human embryonic stem cells in federally funded research, ATP will not consider any proposal that intends to create, destroy, derive, characterize, or use human embryonic stem cells.

H. Research Exempt From the Regulations

Certain research activities may qualify for an exemption from the requirements of the Common Rule. The categories of research that qualify for an exemption can be found at 15 C.F.R. § 27.101(b). The exemptions most commonly cited in ATP awards are the following:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. [15 C.F.R. § 27.101(b)(1)]
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public

behavior, unless (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and (ii) any disclosure of the human subjects' responses outside the research could reasonably place subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. [15 C.F.R. § 27.101(b)(2)]

3. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. [15 C.F.R. § 27.101(b)(4)]

Exemptions are not available for research involving the protected classes identified at 45 C.F.R. Part 46 Subpart C (prisoners). Also, the exemption at 15 C.F.R. § 27.101(b)(2) for research involving survey or interview procedures or observation of public behavior does not apply to research with children, except for research involving observations of public behavior when the investigator or investigators do not participate in the activities being observed.

To determine whether your research qualifies for an exemption from the Common Rule or 45 C.F.R. Part 46 Subparts B or D, please see the Human Subjects Determination Checklist in Appendix 2.

I. Required Documentation

You are required to indicate on Form NIST-1262 or Form NIST-1263, at item 13.D in the *ATP Proposal Preparation Kit,* whether your research involves human subjects.

The Human Subjects Determination Checklist in Appendix 2 will assist you in determining whether your research involves human subjects. You are strongly encouraged to review the authorities found in Appendix 2 before submitting your Gate 1 proposal.

NIST and ATP reserve the right to make an independent determination of whether your research involves human subjects. If NIST or ATP determines that your research project includes human subjects, you will be required to provide additional information for review and approval.

The documentation requirements for the use of human subjects are listed below. In addition, a timeline for the submission of required documents is presented in Appendix 5.

1. Research Exempt From the Common Rule

If your use of human subjects qualifies for an exemption from the Common Rule, you are required to submit a completed exemption request form (see Appendix 3 or 4, as applicable) with your Gate 1 proposal.

2. Research Not Exempt From the Common Rule

If your use of human subjects does not qualify for an exemption, and the research is scheduled to begin during the first year, you are required to submit the following at Gate 3:

a. a signed copy of the final Institutional Review Board (IRB) approved human subjects research protocol for each of the specific research tasks;

b. a copy of all IRB approved consent forms and advertisements;

c. a signed and dated approval letter from the IRB that indicates the start and end dates for the approved research; and

d. if applicable, any IRB required interim reporting requirements.

3. Research Beginning After Year 1 of the Proposal

If there are no research tasks involving human subjects in the first year of the proposal, but there are tasks anticipated beyond the first year, a detailed request for deferred IRB approval or exemption as appropriate under 15 C.F.R. § 27.118 must be submitted to ATP at Gate 1. A deferral request must include the following information:

a. an outline of the tasks that will be performed using human subjects;

b. the projected start date for the use of human subjects (e.g., second quarter of year 3);

c. an outline of when the ATP and NIST required documentation will be submitted to ATP for review and approval; and

d. if the research requires IRB review and approval, the name of the institution housing the IRB and the assurance number on file with OHRP.

J. Contact Information

If you have any questions regarding the use of human subjects in research, please call the ATP Human and Animal Subjects Advisor at 301–975–8779.

The information contained in this booklet is also available on the ATP website at http://www.atp.nist.gov/atp/helpful.htm.

K. Definitions

Terms used in this booklet are defined in the Common Rule at 15 C.F.R. Part 27.

The regulations under 15 C.F.R. Part 27 can be found at http://www.doc.gov/oebam/gforms.htm.

Clinical Trial: A prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

Custom Collection: The collection or gathering of organs, tissues, cells, or data for the purpose of research that would have otherwise not been collected or gathered.

Human Subject: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information. [15 C.F.R. § 27.102(f)]

The regulations governing human subjects extend to the use of human organs, tissues, cells, and bodily fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects.

Intervention: Includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. [15 C.F.R. § 27.102(f)]

Phase I Clinical Trial: A clinical trial done to test a new biomedical or behavioral intervention in a small group of people (e.g., 20–80) for the first time to evaluate safety, efficacy, and effectiveness (e.g., determine a safe dosage range and identify side effects).

Private Information: Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [15 C.F.R. § 27.102(f)]

Research: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. [15 C.F.R. § 27.102(d)]